REMARKS

Claims 7, 10 and 13-15 are pending in the present application and stand ready for further examination on the merits. Support for new claims 13-15 can be found at page 2 and 3 of the instant specification. Support for the amendment to claim 7 can be found in claim 12 and line 1 of page 3. No new matter has been added, and there is no need for further search.

Request For Withdrawal of Finality

Applicants respectfully submit that the Examiner has incorrectly made final the outstanding Office Action. The outstanding Office Action contains a new ground of rejection **not** necessitated by amendment, i.e., the rejection under 102(b) over Modi et al. Therefore, the Office Action is not permitted to be made Final, see MPEP 706.07(a).

Applicants respectfully submit that entry of this amendment is currently a matter of right under 37 CFR 1.111 (since the amendment contains no new matter). However, should the Examiner maintain the finality of the outstanding Office Action, then Applicants further submit that this amendment raises no new issues and directly addresses points raised in the outstanding Office Action, thus, placing the application into better form for appeal, if necessary. Accordingly, the amendment should be considered and entered of record under 37 CFR 1.116.

Withdrawn Rejections

Applicants note with appreciation that the Examiner has indicated the withdrawal of the rejections under 35 USC 112, first, second and fourth paragraphs, and the rejection of claims 1-6 under 35 USC 102(b) over Gomi et al or Michalevicz.

Rejections Over Gomi et al

Claims 7 and 9-11 stand rejected under 35 USC 102(b) as being anticipated by Gomi et al **and** claims 7 and 9-11 stand rejected under 35 USC 103 as being unpatentable over Gomi et al. Applicants respectfully traverse the rejections.

Regarding the Rejection under 35 USC 102 -

Gomi et al teach that ReIFN-γ and ReIFN-β are active against human osteosarcoma G-292 cells. Applicants submit that the claims are not drawn to a method of treating osteosarcoma. Furthermore, there is no teaching or suggestion by Gomi et al that ReIFN-γ and ReIFN-β are useful in treating "multiple myeloma or a bone metastasis from mammary carcinoma, lung cancer, prostate cancer, thyroid gland carcinoma, renal cancer, colon cancer, cancer of the digestive tract, or cancer of the esophagus". Thus, Applicants respectfully request the rejection under 35 USC 102(b) be withdrawn.

Regarding the Rejection under 35 USC 103 -

Applicants respectfully submit the Examiner has used flawed logic in finding Gomi et al makes the instantly claimed invention obvious. The Examiner states,

> "However, Gomi et al differ from instant invention in failing to disclose a bone disorder which is a bone metastasis from other tumors. Applicants admit in Background art section that bone formation and resorption is disturbed including cancer-related diseases such as bone metastasises of lung cancer, mammary carcinoma or renal cancer…
>
> It would have been *prima facia* obvious for one of the ordinary skill in the art at the time the invention was made to use the method of treating bone disorder disclosed by Gomi et al. One of ordinary skill in the art would have been motivated to substitute treatment of bone metastasises from various cancers for Gomi et al's treatment of osteosarcoma by IFN-beta because one of ordinary skill in the art would have recognized that IFN beta would function in the same manner on all bone related tumor cells in providing a treatment of a bone disorder."

The disclosure of Gomi et al is limited to the antitumor activity of ReIFN-β and ReIFN-γ for treating osteosarcoma G-292 cells. There is no teaching or suggestion that these compounds affect the proliferation and/or resorption of normal bone cells. Thus, relevant to claims 13-15, treatment of disorders not related to tumors is not disclosed or suggested by Gomi et al.

Furthermore, the skilled artisan, cognizant that bone cell proliferation and resorption is disturbed in cancer-related diseases and that ReIFN-β and ReIFN-γ are useful in treating cancers such as osteosarcoma, would not come to the reasonable conclusion that ReIFN-β or ReIFN-γ would be useful to treat any and all cancer localized in bone. One would especially <u>not</u> learn

from Gomi et al. that metastases of tumors originating in tissues other than bone would be responsive to ReIFN-β or ReIFN-γ. For example, at page 887, Gomi et al. states that the anti-tumor activity of IFN-β or IFN-γ "is presumed to be mediated by direct anticellular activity, but not by immunological activity" and admits that the antitumor effect against cell types other than osteosarcoma must be tested. Thus, Gomi et al. fails to establish any expectation that metastases from other primary tumors, for example, mammary carcinoma, express cell surface receptors for IFN-β or IFN-γ and so would respond to treatment with these cytokines.

Simply put, there is a fatal gap between the teachings of Gomi et al., the alleged admission (as found in the paragraph bridging pages 2 and 3) and the claimed invention, such that a skilled artisan could not find the instantly claimed invention obvious. The combination of the instant disclosure and Gomi et al differ from the instantly claimed invention in two critical aspects: 1) ReIFN-β or ReIFN-γ have not been shown to engender the healing of normal bone material damaged by cancer; and/or 2) ReIFN-β or ReIFN-γ have not been shown to directly treat the cancers of multiple myeloma, bone metastasis from mammary carcinoma, lung cancer, prostate cancer, thyroid gland carcinoma, renal cancer, colon cancer, cancer of the digestive tract, and cancer of the esophagus. By not addressing this gap, the Examiner appears to be using improper hindsight reconstruction.

> "It is wrong to use the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit." Orthopedic Equip. Co. v. United States, 217 U.S.P.Q. 193 (Fed. Cir. 1983).

Thus, the instantly claimed invention is not made obvious by Gomi et al. Applicants respectfully request the rejection be withdrawn.

Rejections Over Modi

Claims 7 and 9-11 stand rejected under 35 USC 102(b) as being anticipated by Modi US 5,417,982. Claim 11 is cancelled, rendering the rejection moot to that claim. Applicants respectfully traverse the rejection as applicable to claims 7, 9; 10 and 13-15.

The disclosure the Examiner is relying on is found in lines 62-68 of column 4 and reads as follows,

> "The present invention may be used to entrap other growth hormones in a polymer matrix, e.g. estrogens, androgens, insulin, IGF, interleukin-I and interleukin-II. Cytokins such as *interferon*-β and *interferon*-γ, used in the treatment of diseases such as *osteoporosis*, diabetes mellitus and multiple sclerosis may also benefit from the present invention." (emphasis added)

The disclosure of Modi is concerned with the controlled release of drugs or hormones in biodegradable polymer microspheres.

For a reference to properly anticipate a claimed invention, the reference must enable the skilled artisan to make and use the invention. *Akzo N.V. v. International Trade Commission*, 1 USPQ2d 1241, 1245 (Fed. Cir. 1986); *In re Donohue*, 226 USPQ 619 (Fed.

Cir. 1985). Modi clearly lacks enablement; thus, Modi is not sufficient to anticipate or render obvious the claimed invention.

Modi does not enable the skilled artisan to treat any disease with a composition comprising IFN-β or IFN-γ. Modi merely presents a wish to treat one specific bone disorder with such a composition. The disclosure is severely limited in view of the ultimate *in vivo* goal of the invention. Modi does not provide any *in vivo* data, and merely shows that a coating consisting of starch and ethylhydroxycellulose will release either myoglobin or FHSA over a period of up to 120 days in a distilled water solution as measured by UV absorbance. There is no clear guidance as to what modifications to the exemplified coatings are required for *in vivo* application of the much smaller, and therefore diffusable, IFN peptides.

Also, Modi's disclosure does not provide adequate guidance for treating osteoporosis with IFN-β or IFN-γ in that it does not include any direction regarding dosage or route of administration. Thus, Modi clearly lacks enablement of Applicants' claimed invention. Accordingly, Applicants respectfully request the instant rejection over Modi be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, the invention as instantly claimed is in condition for allowance. A Notice to such effect is earnestly solicited. In the event that the amendment does not place the present application into

condition for allowance, entry thereof is respectfully requested as placing the present application into better condition for appeal.

In the event there are any additional matters remaining in this application, the Examiner is strongly encouraged to contact the undersigned, at (703) 205-8000 in order to discuss these matters.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of two (2) months to November 10, 1998, in which to file a reply to the Office Action. The required fee of $400.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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